

**REMARKS/ARGUMENTS**

Upon entry of this reply, claims 3-15 and 31, will remain pending with claim 31 being the sole independent claim.

Reconsideration and allowance of the application are respectfully requested.

**Restriction Requirement**

Applicants note that claims 3-15 and 31 drawn to a carrier having immobilized antibodies are under consideration in the instant application.

In response, Applicants once again respectfully submit that the requirement is improper, because antigens and antibodies should not be separate groups of invention, but are, in fact, species of the broadly recited antigen or antibody in the independent claim. Prosecution of species of antigen and antibody is appropriate in the instant application. Therefore, upon allowance of a generic claim, claims directed to non-elected species should be rejoined.

Accordingly, reconsideration and withdrawal of the Restriction Requirement is respectfully requested.

**Response To Rejection Based Upon Prior Art**

The following rejection is the sole prior art rejection that has been maintained in the Office Action:

Claims 3-15 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kitano et al. (hereinafter "Kitano"), GB 2,282,548, or Mitoh et al. (hereinafter "Mitoh"),

GB 2,307,552, each in view of Nakayama et al. (hereinafter "Nakayama"), U.S. Patent No. 5,827,669, and further in view of Johnson et al. (hereinafter "Johnson"), U.S. Patent No. 4,885,207.

In response to the above-noted grounds of rejection, Applicants respectfully submit the following:

Applicants independent claim 31 is directed to a carrier having immobilized antigens or antibodies, comprising:

a carrier having a substantially spherical shape and having a surface, wherein at least the surface of the carrier is formed of a calcium phosphate based compound;

antiligands provided on the surface of the carrier;

a blocking layer formed of a protein having low interaction with antigens or antibodies and having a metallic ion which has been subjected to a treatment for removing or reducing the metallic ion, the blocking layer being located on at least a portion of the surface of the carrier where the antiligands are not provided; and

antigens or antibodies each having a constant region on which a ligand is provided, each of said antigens or antibodies being immobilized to the surface of the carrier through bonding between the ligands and antiligands with the blocking layer effectively preventing antigens or antibodies from being directly absorbed to the surface without bonding between the ligand and the antiligands.

The features of Applicants' claims have been thoroughly discussed in Applicants' previously filed responses, including the Amendment Under 37 C.F.R. 1.116, filed June 30, 2004, and the Amendment Under 37 C.F.R. 1.111, filed January 4, 2005.

Accordingly, for the sake of brevity these arguments are not being repeated herein but

are incorporated by reference as if set forth in their entirety. However, Applicants note that for the reasons previously advanced by Applicants, Applicants respectfully submit that one having ordinary skill would not combine Kitano, Mitoh, Nakayama and/or Johnson in any manner to arrive at Applicants' disclosed and claimed invention. For example, there is no motivation in the prior art to combine the disclosures of the documents utilized in the rejection of record to arrive at Applicants' invention.

Moreover, Applicants note that claim 31 recites, amongst other features, a blocking layer formed of a protein having low interaction with antigens or antibodies and having a metallic ion which has been subjected to a treatment for removing or reducing the metallic ion, the blocking layer being located on at least a portion of the surface of the carrier where the antigens are not provided. According to this structure, the protein coating for the surface of the carrier can be made to a substantially complete one, as disclosed at page 20, lines 18-23. Applicants respectfully submit that the prior art utilized in the rejection of record does not teach or suggest this aspect of Applicants' invention. Accordingly, for this additional reason no combination of the prior art teaches or suggests Applicants' subject matter as recited in claim 31.

In response to Applicants' arguments, the Final Office Action contends that the statements in the rejection regarding the blocking layer formed of a protein having low interaction with antigens or antibodies and having a metallic ion which has been subjected to a treatment for removing or reducing the metallic ion are not based upon a naked assertion. The Final Office Action asserts that the rejection is based upon the disclosure of Applicants' specification wherein it is disclosed that casein is well known to be one of the metallic proteins that can be treated to remove or reduce the metallic ion.

The rejection contends that both the prior art and the instant specification use casein only as a blocking agent to cover the portion of the surface of the carrier to prevent unspecific bonding to the carrier and the specification does not teach any advantage of using treated casein as a blocking agent compared with untreated casein.

In response to these assertions, Applicants initially note that the question is not what Applicants' specification discloses, but what the prior art discloses. The Examiner is reminded that Applicants' disclosure of certain blocking agents does not constitute prior art. The rejection must show that the prior art includes motivation for arriving at Applicants' invention.

In particular, Applicants disclose at page 19, line 12 through page 21, line 8:

By providing such a protein coating, it becomes possible to effectively prevent the antibodies from being unspecifically adsorbed to the carrier when the antibodies are immobilized to the carrier. Namely, it is possible to prevent that the antibodies are adsorbed to the carrier directly without using the ligands and antiligands. As a result, the carrier having immobilized antibodies can have an increased antigen bonding ability.

Further, when detection for antigens which have a characteristic to be adsorbed to a calcium phosphate compound is carried out using the obtained carrier having immobilized antibodies, it is possible to prevent the antigens from being unspecifically bonded (adsorbed) to the carrier.

As for the protein, any protein having a characteristic to be adsorbed to a calcium phosphate compound is preferably used. Namely, it is preferable that a portion of the surface of the carrier to which the antibodies are not immobilized is covered by a protein by the adsorption of the carrier to the surface of the carrier. By using such a protein, it becomes possible to cover the outer surface of the carrier with the protein by means of a simple method such as only contacting the protein to the carrier (described later in more detail).

Examples of such a protein include metallic proteins such as casein, transferin, ferredoxins, and the like, albumin, gelatin, vitellin, phosvitin, and the like. Among these proteins, casein, albumin and gelatin are preferably used. These proteins have excellent adsorptivity to calcium phosphate

compounds. Further, among these proteins, casein is most preferable, since casein has excellent adsorptivity to calcium phosphate based compounds and has extremely small interaction with antibodies.

Further, when a protein having a metallic ion such as metallic protein or the like is used, it is preferable that the protein has been subjected to a treatment for removing or reducing the metallic ion. By this treatment, the protein coating for the surface of the carrier can be made to a substantially complete one.

As for a method for removing the metallic ion, a method in which a solution of such a protein (blocking agent solution) is processed by a chelating agent such as ethylene-diamine tetra-acetate (EDTA) can be mentioned. In this case, as for an example of the treatment of the protein solution with the chelating agent, the following method can be mentioned. Namely, after a chelating agent is added to a protein solution, the chelating agent is removed from the protein solution by means of a gel filtering, an ultrafiltration, or a dialysis, or the like.

In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. In the instant situation, the rejection points to the above disclosure in Applicants' specification which discloses proteins, and an improvement in the use of proteins wherein the metallic ion therein is removed or reduced. Moreover, the rejection points to blocking agents, such as casein, in the prior art which include metallic ions therein. However, the rejection does not point to any documentary evidence for removing or reducing the metallic ion in the casein in the prior art. Certainly, Applicants' recited structure would be different from the structure disclosed in the prior art, because the casein in the prior art would not have removed or reduced metallic ion.

Moreover, such structure associated with Applicants' invention, by removing or reducing metallic ions, such as calcium ion, contained in the protein, permits calcium ion

contained in calcium phosphate (which forms at least part of the carrier) to more easily bond with the protein, whereby the carrier can be coated with the protein without leaving any portions of the calcium phosphate where no protein is adsorbed.

With regard to the above, the Examiner is once again reminded that Applicants' disclosure, at page 20, lines 18-23, discloses, "Further, when a protein having a metallic ion such as metallic protein or the like is used, it is preferable that the protein has been subjected to a treatment for removing or reducing the metallic ion. By this treatment, the protein coating for the surface of the carrier can be made to a substantially complete one. (Emphasis added)." Therefore, Applicants' claimed carrier is advantageous, and is not taught or suggested by the prior art of record.

Applicants further respectfully submit that an obviousness rejection cannot be supported by mere allegations that it would have been obvious to arrive at Applicants' invention. The Examiner is reminded that a rejection must be based upon documentary evidence, and not merely official notice. In this regard, the Examiner's attention is directed to MPEP 2144.03 wherein it is noted that, "If the applicant traverses such an assertion the examiner should cite a reference in support of his or her position".

In the instant situation, Applicants respectfully submit that the rejection is improper as not utilizing documentary evidence to support the position taken in the rejection. The rejection merely makes an assertion of obviousness "that casein is well known to be one of the metallic proteins that can be treated to remove or reduced the metallic ion", but does not support assertion of removing or reducing metallic ion in the protein by documentary evidence. The rejection merely improperly refers to Applicants' disclosure.

There is not the slightest documentary evidence to arrive at Applicants' disclosed and claimed invention.

Moreover, attention is directed to In re Ahlert and Kruger, 424 F.2d 1088, 165 USPQ 418, 420-421 (CCPA 1970), which is cited in MPEP 2144.03. In Ahlert, at 165 USPQ 421, it is stated that:

Typically, it is found necessary to take notice of facts which may be used to supplement or clarify the teaching of a reference disclosure, perhaps to justify or explain a particular inference to be drawn from the reference teaching. The facts so noticed serve to "fill in the gaps" which might exist in the evidentiary showing made by the examiner to support a particular ground of rejection. We know of no case in which facts judicially noticed comprised the principal evidence upon which a rejection was based or were of such importance as to constitute a new ground of rejection when combined with the other evidence previously used.

In the instant case, the rejection improperly utilizes an assertion, which can at best be characterized to be considered Official Notice, not to "fill in the gaps", but to provide a complete reasoning behind modification of the primary reference. Accordingly, Applicants submit that it is improper to make such naked assertion in the instant case, and a reference must be utilized in the rejection that not only discloses Applicants' recited concept, but also provides motivation for modifying the documents to include Applicants' recited features. This would afford Applicants an opportunity to address issues of lack of motivation for combining separate disclosures as well as an opportunity to argue against any asserted combination.

Thus, in the unlikely event that the rejection is maintained, Applicants request that the rejection be modified to include documentary evidence supporting the position taken in the rejection, and that the rejection not be based upon a naked assertion of obviousness or an assertion of obvious to try.

Still further, it is noted that the rejection appears to be asserted that casein is a metallic protein that can be treated to remove or reduce the metallic ion as claimed. Whether or not a metallic ion can be removed or reduced is not the question to be address in the rejection, the rejection must address whether one having ordinary skill in the art would have been motivated to modify the prior art to arrive at Applicants' invention. In the instant situation, the rejection is silent with respect to any such motivation in the prior art, and merely (and improperly utilized) Applicants' disclosure.

Thus, Applicants once again respectfully submit that the only teaching or suggestion that would lead one having ordinary skill in the art to arrive at Applicants' invention is within Applicants' disclosure, and the use of such disclosure by the Examiner is improper. In order to support the conclusion that the claimed invention is either anticipated or rendered obvious over the prior art, the prior art must either expressly or inherently teach the claimed invention or the Examiner must present a convincing line of reasoning why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references. Ex parte Clapp, 227 U.S.P.Q. 972 (B.O.A. 1985).

Additionally, each of the dependent claims is patentable over the prior art of record in view of the fact that each of these dependent claims includes the limitations of the independent claim. Moreover, each of the dependent claims is patentable over the prior art of record because it would not have been obvious to one having ordinary skill in the art to incorporate such dependent claim features into the invention as more broadly recited in the independent claim.



In view of the above, the rejection of record should be withdrawn, and all of the pending claims indicated to be allowable.

### CONCLUSION

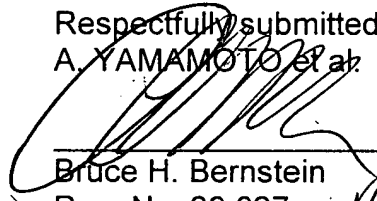
In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the objections and rejections of record, and allow each of the pending claims.

Applicants therefore respectfully request that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

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